Summary of Recommendations

Recommendations for Prevention and Control of Infections in NICU Patients: *S. aureus* (2020)

AT A GLANCE

Summary of Recommendations from the Recommendations for Prevention and Control of Infections in NICU Patients: *S. aureus* (2020) guideline.

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Recommendation 1.a.

Recommendation

Perform active surveillance testing for S. aureus colonization in neonatal intensive care unit patients when there is an increased incidence of S. aureus infection or in an outbreak setting. (**Recommendation)**

- ***Supporting Evidence:*** The evidence consists of ten observational studies.[2–11]
- ***Level of Confidence in the Evidence:*** The level of confidence in this evidence is low because observational studies are considered to be at higher risk of bias than randomized controlled trials.
- ***Benefits:*** When there is an increased incidence of *aureus* infection or in an outbreak setting, the benefit of performing active surveillance testing for *S. aureus* colonization in NICU patients is a reduction in *S. aureus* infection, colonization, and transmission resulting from facility implementation of strategies targeting patients identified by active surveillance testing.
- ***Risks and Harms:*** Harms that could result from performing active surveillance testing in this population and setting include minor patient discomfort from performing nasal swabs or bleeding caused by trauma to the nasal mucosa. The institution of Contact Precautions has inconsistently been associated with unintended consequences, such as decreased healthcare personnel-patient contact, in other populations. [12–16] This literature search did not identify studies suggesting harm from use of Contact Precautions in NICU populations.

- ***Resource Use:*** Implementing active surveillance testing will result in increased human and material costs; however, it is anticipated that these costs will be less than the cost associated with invasive *aureus* infections in this vulnerable population that could be prevented by subsequent implementation of additional infection prevention strategies.
- ***Balance of Benefits and Harms:*** There is a preponderance of benefit over harm for active surveillance testing for *aureus.*
- ***Value Judgments:*** Infection prevention, patient safety, and outbreak management in this high-risk population were all considered in the formulation of this recommendation.
- ***Intentional Vagueness:*** The term " *aureus"* includes both methicillin-sensitive *S. aureus* (MSSA) and MRSA. An "increased incidence *of S. aureus* infection" may include a cluster of *S. aureus* infections or an increase in the endemic incidence of *S. aureus* infection compared to historical data from the unit or the published literature.
- ***Exceptions:*** There are no exceptions to this recommendation.

Recommendation 1.b.

Recommendation

Perform active surveillance testing for methicillin-resistant *S. aureus* (MRSA) colonization in neonatal intensive care unit patients when there is evidence of ongoing healthcare-associated transmission within the unit. **(Recommendation)**

- ***Supporting Evidence:*** The evidence consists of five observational studies.[3,4,6–8]
- ***Level of Confidence in the Evidence:*** The level of confidence in this evidence is low because observational studies are considered at higher risk of bias than randomized controlled trials.
- ***Benefits:*** Implementation of active surveillance testing for MRSA colonization when there is evidence of ongoing healthcare-associated transmission could lead to the prompt implementation of infection control strategies that will result in a reduction of person-to person transmission and decreased incidence of MRSA colonization and infection.
- ***Risks and Harms:*** Harms that could result from performing active surveillance testing in this population and setting include minor patient discomfort from performing nasal swabs or bleeding caused by trauma to the nasal mucosa. The institution of Contact Precautions has inconsistently been associated with unintended consequences, such as decreased healthcare personnel-patient contact, in other populations.12-16 This literature search did not retrieve data suggesting harm from use of Contact Precautions in NICU populations.
- ***Resource Use:*** Implementing active surveillance testing for MRSA colonization will result in increased human and material costs; however, it is anticipated that these costs will be less than the cost associated with MRSA infections in this vulnerable population that could be prevented by subsequent implementation of additional infection prevention strategies.
- ***Benefit-Harm Assessment:*** There is a preponderance of benefit over harm for active surveillance testing for MRSA.
- ***Value Judgments:*** Values considered in the formulation of this recommendation include patient safety and resource considerations.
- ***Intentional Vagueness:*** "Healthcare-associated transmission within the unit" is suggested by an increase in cases of MRSA colonization or infection as determined by surveillance cultures or cultures obtained for clinical indications.
- ***Exceptions:*** This recommendation only applies to MRSA.

Recommendation 1.c.

No Recommendation

The use of active surveillance testing for methicillin-sensitive *S. aureus* (MSSA) colonization in neonatal intensive care unit patients to detect ongoing healthcare-associated MSSA transmission is an unresolved issue. **(No Recommendation)**

- ***Supporting Evidence:*** No evidence was retrieved evaluating the use of active surveillance testing for MSSA colonization in NICU patients to prevent transmission of MSSA.
- ***Level of Confidence in the Evidence:*** This criterion is not applicable.
- ***Benefits:*** If a facility chooses to implement active surveillance testing for MSSA, it is likely that interventions subsequently implemented to reduce MSSA transmission would result in a decrease in MSSA infections in other NICU patients.
- ***Risks and Harms:*** Harms that could result from performing active surveillance testing in this population and setting include minor patient discomfort from performing nasal swabs or bleeding caused by trauma to the nasal mucosa. If facilities choose to conduct active surveillance for MSSA colonization in NICU patients, there may be minor patient discomfort from performing nasal swabs.
- ***Resource Use:*** There would be no additional resource use if facilities chose not to conduct active surveillance for MSSA; however, if facilities chose to conduct active surveillance for MSSA to implement interventions to reduce MSSA infection and colonization, there would be increased human and material costs.
- ***Benefit-Harm Assessment:*** MSSA can be pathogenic and can cause invasive infections; however, benign colonization with MSSA without associated clinical signs of invasive infection is common in NICU patients. Active surveillance testing may identify infants at risk to develop MSSA infection and who may be the source for transmission of MSSA to other infants. The optimal strategies to decrease individual risk and risk to the population from MSSA-colonized infants remains unresolved.
- ***Value Judgments:*** Values considered in the formulation of this recommendation include the availability of evidence, patient safety, and resource considerations.
- ***Intentional Vagueness:*** "Healthcare-associated transmission within the unit" is suggested by an increase in cases of MSSA colonization or infection as determined by cultures obtained for clinical indications.
- ***Exceptions:*** This recommendation only applies to MSSA.

Recommendation 1.d.

Recommendation

If active surveillance testing for S. aureus colonization is implemented for neonatal intensive care unit patients, test at regular intervals to promptly identify newly colonized patients. (**Recommendation)**

- ***Supporting Evidence:*** The evidence consists of ten observational studies.[2–4,6–11,17]
- ***Level of Confidence in the Evidence:*** The level of confidence in this evidence is low because observational studies are considered to be at higher risk of bias than randomized controlled trials.
- ***Benefits:*** Implementation of routine active surveillance testing for *aureus* colonization will enable facilities to identify colonized patients promptly and guide implementation of appropriate infection prevention and control measures to reduce person-to-person transmission.
- ***Risks and Harms:*** Harms that could result from performing active surveillance testing in this population and setting include minor patient discomfort from performing nasal swabs or bleeding caused by trauma to the nasal mucosa.
- ***Resource Use:*** The frequency of testing will directly affect costs, including human and laboratory resource costs.
- ***Benefit-Harm Assessment:*** There is a preponderance of benefit over harm for testing routinely for *aureus* colonization in NICU patients.
- ***Value Judgments:*** Values considered in the formulation of this recommendation include patient safety and resource considerations.
- **Intentional Vagueness:**
  - The frequency of active surveillance testing is noted as "at regular intervals" to allow facilities to sample weekly, or more or less frequently, depending upon the facility's baseline rates of colonized and infected patients or as unit epidemiology changes.
  - The addition of admission testing to testing at regular intervals is best determined by the individual facility or health system.

- **Exceptions:** There are no exceptions to this recommendation.

Recommendation 1.e.

Conditional Recommendation

If active surveillance testing for *S. aureus* colonization in neonatal intensive care unit patients is implemented, consider testing outborn infants or infants transferred from other newborn care units on admission to promptly identify newly admitted colonized patients. **(Conditional Recommendation)**

- ***Supporting Evidence:*** The evidence consists of four observational studies.[2,8–10]
- ***Level of Confidence in the Evidence:*** The level of confidence in this evidence is low because observational studies are considered to be at higher risk of bias than randomized controlled trials. Additionally, three of the four studies were conducted in the same facility, potentially limiting the generalizability of their results.
- ***Benefits:*** If outborn infants or infants transferred from other newborn care units are tested on admission for *aureus* colonization, a reduction in *S. aureus* colonization and infection could be seen due to potentially higher endemic rates in the outborn neonatal population.
- ***Risks and Harms:*** If facilities chose to conduct active surveillance for *aureus* colonization in NICU patients, there could be minor patient discomfort from performing nasal swabs or bleeding caused by trauma to the nasal mucosa.
- ***Resource Use:*** Performing testing for *aureus* colonization on outborn infants or infants transferred from other newborn care units on admission would result in increased material and human resource costs. However, it is anticipated that these costs will be less than the cost of invasive *S. aureus* infections in this vulnerable population that could be prevented by subsequent implementation of additional infection prevention strategies.
- ***Benefit-Harm Assessment:*** There is a preponderance of benefit over harm for testing outborn infants or those transferred from other newborn care units. Relatively minor risks and harms, including discomfort from performing nasal swabs and the costs of testing, are outweighed by the potential benefits of preventing *aureus* colonization and infection. The likelihood of benefit increases in settings in which outborn and transferred infants have higher *S. aureus* colonization rates.
- ***Value Judgments:*** Values considered in the formulation of this recommendation include patient safety and economic and human resource costs.
- ***Intentional Vagueness:***
  - Benefit has also been seen in the literature in testing all neonates on admission. The recommendation specifies outborn infants or transferred infants because the literature showed a higher colonization prevalence in this population compared to newborns admitted from labor and delivery units. Units can consider their own unique epidemiologic needs when determining the optimal population to test on admission.
  - The term " *aureus"* includes methicillin-resistant *S. aureus* (MRSA) and methicillin-sensitive *S. aureus* (MSSA).
- ***Exceptions:*** There are no exceptions to this recommendation.

Recommendation 1.f.

Recommendation

If active surveillance for S. aureus colonization in neonatal intensive care unit patients is performed, either culture-based or polymerase chain reaction detection methods are acceptable. **(Recommendation)**

- ***Supporting Evidence:*** The evidence consists of three diagnostic studies.[18–20]
- ***Level of Confidence in the Evidence:*** The level of confidence in this evidence is moderate due to imprecision in the estimate of effect.

- ***Benefits:*** If this recommendation is followed, facilities will be able to select the assay that best fits facility considerations and the needs at hand. While polymerase chain reaction (PCR) testing offers marginally increased sensitivity over culture for detecting *S. aureus*, culture has the advantage of having isolates available for molecular typing and susceptibility tests.

- ***Risks and Harms:*** PCR is more sensitive for the detection of *S. aureus* and offers a small additional benefit over culture. PCR can have a more rapid turnaround, depending on laboratory capabilities; however, PCR has a lower specificity for detecting methicillin-resistant *S. aureus* (MRSA). While culture is not likely to miss detecting a large number of *S. aureus*-colonized infants, the possibility exists that the use of culture-based methods may result in a small number of *S. aureus*-colonized infants not being identified. PCR does not yield organisms that can undergo strain typing, which is a disadvantage in an outbreak investigation.
- ***Resource Use:*** PCR is more expensive than culture-based methods.
- ***Benefit-Harm Assessment:*** There is a benefit to using PCR versus culture-based methods to detect *S. aureus* colonization, but this benefit is offset by important considerations. The sensitivity of PCR is slightly higher, but facilities can balance performance characteristics of the test, clinical management considerations, susceptibility testing, facility volume, outbreak identification, and test turnaround time when choosing an assay, as outlined above.
- ***Value Judgments:*** Values considered in the formulation of this recommendation include test characteristics and availability, outbreak management, unit volume, economic considerations, need for a full susceptibility panel, speed of test turnaround, and resource utilization.
- ***Intentional Vagueness:*** The term "*S. aureus"* incudes MRSA and methicillin-sensitive *S. aureus* (MSSA).
- ***Exceptions:*** There are no exceptions to this recommendation.

Recommendation 1.g.

Recommendation

If active surveillance for S. aureus colonization of neonatal intensive care unit patients is performed, collect samples from at least the anterior nares of neonatal intensive care unit patients. **(Recommendation)**

- ***Supporting Evidence:*** The evidence consists of two diagnostic studies.[21,22]
- ***Level of Confidence in the Evidence:*** The level of confidence in this evidence is moderate due to inconsistent results across studies.
- ***Benefits:*** The anterior nares have the highest yield for identifying *aureus* colonization. Collecting samples from the axilla, rectum, and umbilicus can increase the yield. The yield from collecting samples from additional sites offers an incremental increase in sensitivity. During outbreaks with a highly virulent strain, sampling additional sites might provide greater benefit.
- ***Risks and Harms:*** Harms that could result from performing active surveillance testing in this population and setting include minor patient discomfort from performing nasal swabs or bleeding caused by trauma to the nasal mucosa. Further, if neonates are not colonized in the anterior nares and only the nares are sampled, then colonization at another anatomic sites may be missed.
- ***Resource Use:*** There could be increased costs associated with running multiple assays for multiple sites, including time, financial, human, and material resources. However, samples could be combined and processed as a single test to yield a composite result, limiting increased costs associated with sampling multiple sites.
- ***Benefit-Harm Assessment:*** There is a preponderance of benefit over harm for sampling at least the anterior nares, which is the most sensitive anatomic site for identifying NICU patients colonized with *aureus.* However, some infants are colonized at sites other than the anterior nares, and those infants would be missed if only the nares were sampled. No patient-level harm is associated with sampling the axilla, rectum, or umbilicus: only additional resource utilization and cost. While collecting samples from additional sites increases sensitivity, it is not clear that the additional samples will have a meaningful impact on outcomes, or that the additional costs are warranted. The benefit of testing additional sites may be greater in periods in which increased sensitivity is needed, such as during an outbreak.
- ***Value Judgments:*** Values considered in the formulation of this recommendation include test characteristics and resource utilization.
- ***Intentional Vagueness:*** The term " *aureus"* includes methicillin-resistant *S. aureus* (MRSA) and methicillin-sensitive *S. aureus* (MSSA). "At least" is intentionally vague to allow providers to determine alternate sampling sites.

- ***Exceptions:*** There are no exceptions to this recommendation.

Recommendation 2.a.

Conditional Recommendation

Consider targeted decolonization for *S. aureus*-colonized neonatal intensive care unit patients in addition to the implementation of, and adherence to, appropriate infection prevention and control measures in an outbreak setting, or when there is ongoing healthcare-associated transmission, or an increase in the incidence of infection. **(Conditional Recommendation)**

- ***Supporting Evidence:*** The evidence consists of four observational studies.[9–11,23]
- ***Level of Confidence in the Evidence:*** The level of confidence in this evidence is low because observational studies are considered to be at higher risk of bias than randomized controlled trials. Two of these studies were performed in a single center NICU population.
- ***Benefits:*** Implementing targeted decolonization could result in a reduction in the *aureus* colonization rate of NICU patients, which then may result in a reduction in *S. aureus* transmission and infection in NICUs.
- ***Risks and Harms:*** If targeted decolonization were conducted for *aureus* colonized NICU patients, harms could include systemic absorption of decolonizing agents, increased resistance to the decolonizing agent, and adverse skin reactions. Application of nasal ointment can be technically challenging in a very low birth weight infant. There could be minor patient discomfort from the application of intranasal ointment, which could partially occlude small nares and accumulate in the prongs of nasal cannula used to deliver oxygen.
- ***Resource use:*** Conducting targeted decolonization will result in increased material and human resource costs.
- ***Benefit-Harm Assessment:*** The potential reduction in *aureus* colonization resulting from the implementation of targeted decolonization is balanced by concern for the development of antimicrobial resistance, antiseptic tolerance, cross-resistance, and safety concerns due to systemic absorption of decolonization agents seen in this population.
- ***Value Judgments:*** Values considered in the formulation of this recommendation include patient safety, antimicrobial stewardship and resistance concerns, federal regulatory approvals, and resource utilization.
- ***Intentional Vagueness:***
  - While *aureus* colonized NICU patients are the most frequently targeted population for decolonization, the optimal population to target is left for the facility to determine.
  - "Healthcare-associated transmission within the unit" is suggested by an increase in cases of *aureus* colonization or infection as determined by cultures obtained for clinical indications.
  - The term " *aureus"* includes methicillin-resistant *S. aureus* (MRSA) and MSSA.
- ***Exceptions:*** There are no exceptions to this recommendation.

Recommendation 2.b.

No Recommendation

The use of universal decolonization for *S. aureus*-colonized neonatal intensive care unit patients is an unresolved issue. **(No Recommendation)**

- ***Supporting Evidence:*** The evidence consists of two observational studies.[11,17]
- ***Level of Confidence in the Evidence:*** The level of confidence in this evidence is low because observational studies are considered to be at higher risk of bias than randomized controlled trials.

- ***Benefits:*** The implementation of universal decolonization for *aureus* colonized NICU patients could lead to a reduction of *S. aureus* colonization and infection rates.
- ***Risks and Harms:*** Harms associated with implementing universal decolonization in this population include systemic absorption of decolonizing agents and adverse events from the agent chosen for decolonization. Resistance is more likely to develop if decolonization is indiscriminate in its application.
- ***Resource Use:*** If universal decolonization were implemented, resource use would shift from lab costs to decolonization costs, which in some cases may increase or decrease overall resource use.
- ***Benefit-Harm Assessment:*** Universal decolonization may be more feasible and easier to implement than targeted decolonization, but its additional benefit is unclear.
- ***Value Judgments:*** Values considered in the formulation of this recommendation include patient safety, antimicrobial stewardship and resistance concerns, federal regulatory approvals, and resource utilization.
- ***Intentional Vagueness:*** There is no intentional vagueness in this recommendation.
- ***Exceptions:*** There are no exceptions to this recommendation.

Recommendation 2.c.

No Recommendation

The optimal decolonization agent or combination of agents remains an unresolved issue. **(No Recommendation)**

- ***Supporting Evidence:*** The evidence consists of approved labels from the US Food and Drug Administration (FDA) and five observational studies.[9–11,17,23]
- ***Level of confidence in evidence:*** The level of confidence in this evidence is low because observational studies are considered to be at higher risk of bias than randomized controlled trials, and additional evidence is regulatory.
- ***Benefits:*** A reduction is seen in *aureus* infection and colonization when intranasal decolonization is implemented (alone or in combination with antiseptic) in addition to the implementation of core infection prevention and control practices.
- ***Risks and Harms:*** The safety and efficacy of intranasal mupirocin is not established in patients aged less than 12 years. Additionally, in neonates and premature infants, systemic absorption occurs following intranasal administration, but it remains uncertain whether this absorption causes adverse health consequences in neonates. *aureus* may exhibit resistance to mupirocin; increased use of the agent may contribute to increased rates of resistance. The application of a nasal ointment can be technically challenging in a very low birthweight infant and there could be minor patient discomfort from the application of intranasal ointment, which could partially occlude small nares and accumulate in the prongs of nasal cannula used to deliver oxygen. The FDA indication for topical chlorhexidine (CHG) is for use "with care" in premature infants or infants under 2 months of age. The potential harms of CHG in the NICU population retrieved by this review include adverse skin reactions, including chemical burns; systemic absorption of uncertain clinical significance; and the development of tolerance to the agent used, or cross-resistance to other agents.
- ***Resource Use:*** Implementation of decolonization would result in increased material and human resource costs.
- ***Benefit-Harm Assessment:*** The balance of benefits and harms of decolonization agents, which include significant systemic absorption, the development of tolerance to the agent used or cross-resistance to other agents, and topical reactions, is unclear.
- ***Value Judgments:*** Values considered in the formulation of this recommendation include federally approved labels, patient safety, antimicrobial stewardship and resistance concerns, and resource utilization.
- ***Intentional Vagueness:*** This recommendation does not specify a specific decolonization agent or agents because no FDA-approved decolonization agent has been consistently proven effective and safe in this population.
- ***Exceptions:*** There are no exceptions to this recommendation.

Recommendation 3.

No Recommendation

Appropriate procedures to allow discontinuation of Contact Precautions for individual neonatal intensive care unit patients who have a history of colonization or infection with methicillin-resistant *S. aureus* (MRSA) is an unresolved issue. **(No Recommendation)**

- ***Supporting Evidence:*** No evidence was retrieved that could be used to formulate a recommendation regarding appropriate procedures to allow discontinuation of Contact Precautions for individual NICU patients who have a history of colonization or infection with MRSA.
- ***Level of Confidence in the Evidence:*** This criterion is not applicable.
- ***Benefits:*** For patients with a history of *aureus* colonization or infection, continuing Contact Precautions for the duration of hospitalization can prevent transmission of *S. aureus* from patients with recurrent colonization.
- ***Risks and Harms:*** Even after decolonization, neonates can have recurrent *aureus* colonization. Early discontinuation of Contact Precautions for patients with a history of colonization or infection can contribute to increased transmission of *S. aureus*. Implementation of Contact Precautions has inconsistently been associated with unintended consequences, such as decreased healthcare personnel contact, in other populations.[12–16] This literature search did not retrieve data suggesting harm from the use of Contact Precautions in NICU populations.
- ***Resource Use:*** Implementation of Contact Precautions contributes to increased material and human resource costs.
- ***Benefit-Harm Assessment:*** This literature search retrieved no data to support a specific protocol by which to discontinue Contact Precautions (e.g., discontinue after multiple negative cultures).
- ***Value Judgments:*** Values considered in the formulation of this recommendation include patient safety, familial bonding, the individual facility's baseline colonization and infection rates, and economic and human resource considerations.
- ***Intentional Vagueness:*** There is no intentional vagueness in this recommendation.
- ***Exceptions:*** There are no exceptions to this recommendation.

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